

### **REMARKS/ARGUMENTS**

Applicants provide herewith an amendment to the specification and the claims as described above. Support for all amendments is found in the specification as originally filed, and is further discussed below. Other amendments are to correct typographical or clerical errors, support for which is self-evident. Applicants submit that no new matter has been added by way of the above amendment. Accordingly, entry of the amendment is respectfully requested.

The Office Action dated June 16, 2008, included objections to the form of the specification, and claim rejections based on alleged indefiniteness (35 U.S.C. § 112, second paragraph), alleged lack of written description (35 U.S.C. § 112, first paragraph), and alleged anticipation (35 U.S.C. § 102). Applicants traverse all rejections to the extent that they may be applied to the amended claims, for the reasons noted below. The present Response with Amendment is fully responsive to each of the Examiner's points, and Applicants respectfully request reconsideration of the claims in view of the amendments and remarks herein.

### **THE STATUS OF THE CLAIMS**

Claims 1-16 are withdrawn from further consideration. In the Office Action, the Examiner incorrectly states that claims 1-10 and 18-26 are withdrawn from further consideration.

Claims 27-61 are cancelled.

Claims 17-26 are pending and are presently under examination.

Claims 17-21, 25 and 26 are currently amended herein.

This amendment to the claims does not introduce new matter. These amendments are made without prejudice and are not to be construed as abandonment of any originally claimed subject matter or agreement with any objection or rejection of record. Support for the amended claims 17 and 26 is found throughout the specification as originally filed; for example, leucyl-O-tRNA molecules of the invention are listed at paragraphs **0018, 0020, 0075, 0127, 0158** and **0218**. In amended claim 19, the use of leucyl-O-RS species of SEQ ID NOs: 15 and 16 is supported in the specification, for example, at paragraphs **0018** and **0090**.

Aspects of the amendment to claims 18-20, 25 and 26 are to make the language in those claims consistent with the language in amended claim 17 and to improve clarity. Amendment to claims 21 and 26 is to correct a typographical error, where the correct spelling of

*Methanobacterium thermoautotrophicum* is supported in the specification at paragraph 0049, for example.

#### AMENDMENTS TO THE SPECIFICATION

Amendment to paragraphs 0017, 0019 and 0020 are to correct typographical errors of obvious nature.

Amendment to paragraphs 0063, 0097, 0160, 0162 and 0168 are to replace reference to International Application Serial Numbers with International Publication Numbers.

Amendment to other paragraphs are discussed in detail below.

#### COMPLIANCE WITH THE RULES FOR SEQUENCE DISCLOSURES

The Examiner pointed out that the specification on page 67, in Table 1 (paragraph 0193) contains sequence disclosures that are not properly designated with sequence identifier numerals as required under 37 C.F.R § 1.821(c). The Examiner also pointed out that the sequences disclosed in Figures 4 and 5 must be assigned sequence identifier numerals either in the drawing sheets, or alternatively, in the Brief Description of the Figures.

Applicants have amended paragraphs 0054, 0057, 0058, 0074, 0184, 0187 (Table 2) and 0193 (Table 1) to insert sequence identifier numerals. These amended paragraphs include the Brief Description of the Figures for Figures 1, 4 and 5 to designate the sequences that are disclosed on the drawing sheets. This amendment makes the objection moot, and Applicants respectfully request withdrawal of this objection.

#### OBJECTIONS TO THE SPECIFICATION

The Examiner objected to the specification because it contains embedded hyperlinks or browser-executable code at paragraph 0159. Applicants identified additional browser-executable text in paragraphs 0150, 0155 and 0187. Applicants have removed all browser-executable text accordingly. This amendment makes the objection moot, and Applicants respectfully request withdrawal of the objection.

#### 35 U.S.C. § 112, SECOND PARAGRAPH

In the Office Action dated June 16, 2008, claims 17-26 were rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite for failing to define the metes and bounds of the expression “at least about.”

Applicants respectfully disagree, and traverse this rejection. Solely for the purpose of advancing the prosecution of the present application, and without acquiescing to the Examiner's rejection, the Applicants have amended the independent claims 17 and 26. Rebuttal to the Examiner's rejection is made in view of the amended form of claims 17 and 26. The amended forms of these claims no longer recite, "at least about," and furthermore, the expression "at least about" does not appear in any claim that depends on claim 17 or 26.

This amendment renders the rejection moot, and Applicants respectfully request that this rejection be withdrawn.

35 U.S.C. § 112, FIRST PARAGRAPH

In the Office Action dated June 16, 2008, claims 17-26 were rejected under 35 U.S.C. § 112, first paragraph, where the specification allegedly lacks written description for a genus of leucyl-O-tRNA molecules comprising a CU(X)<sub>n</sub>XXXAA consensus and having at least 25% suppression activity compared to a control system lacking a selector codon.

Applicants respectfully disagree, and traverse this rejection. Solely for the purpose of advancing the prosecution of the present application, and without acquiescing to the Examiner's rejection, the Applicants have amended claims 17 and 26. Rebuttal to the Examiner's rejection is made in view of the amended form of claims 17 and 26.

The amended forms of claims 17 and 26 no longer define the genus of leucyl-O-tRNA molecules using the CU(X)<sub>n</sub>XXXAA consensus limitation or the at least 25% suppression activity limitation. The amended forms of claims 17 and 26 now define the members of the genus of leucyl-O-tRNA molecules specifically by structural limitation, *i.e.*, a leucyl-O-tRNA comprising a nucleotide sequence selected from SEQ ID NOS: 1, 2, 4-7 and 12. Each of these members is defined in the specification; see the nucleotide sequences in Example 2 starting at paragraph 0218. Applicants assert that this amendment renders the rejection moot, and Applicants respectfully request that this rejection be withdrawn.

Claim 19 was rejected under 35 U.S.C. § 112, first paragraph, where the specification allegedly lacks written description for "cognate synthetase," and therefore, a genus of O-tRNA/O-RS pairs that are "50% as effective" as a reference O-tRNA/O-RS pair cannot be readily determined.

Applicants respectfully disagree, and traverse this rejection. Solely for the purpose of advancing the prosecution of the present application, and without acquiescing to the Examiner's rejection, the Applicants have amended claim 19. Rebuttal to the Examiner's rejection is made in view of the amended form of claim 19.

The amended form of claim 19 clarifies that the reference cognate synthetase is selected from the O-RS species of SEQ ID NOS: 15 and 16. This amendment removes any perceived ambiguity regarding the reference cognate synthetase that is paired with a leucyl-O-tRNA of SEQ ID NOS: 1, 2, 4-7 or 12. Applicants assert that this amendment renders the rejection moot, and Applicants respectfully request that this rejection be withdrawn.

Claim 19 was rejected under 35 U.S.C. § 112, first paragraph, where the specification allegedly lacks written description for "conservative variant," as it refers to a reference O-RS cognate synthetase in a reference O-tRNA/O-RS pair. Applicants respectfully disagree, and traverse this rejection. Solely for the purpose of advancing the prosecution of the present application, and without acquiescing to the Examiner's rejection, the Applicants have amended claim 19. Rebuttal to the Examiner's rejection is made in view of the amended form of claim 19. The amended form of claim 19 removes the expression "conservative variant." This amendment removes any perceived ambiguity regarding the reference O-RS cognate synthetase that is paired with a leucyl-O-tRNA selected from SEQ ID NOS: 1, 2, 4-7 and 12. Applicants assert that this amendment renders the rejection moot, and Applicants respectfully request that this rejection be withdrawn.

35 U.S.C. § 102(b)

In the Office Action dated June 16, 2008, claims 17 and 23-26 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Thorbjarnardóttir *et al.* (1985) "Leucine tRNA Family of *Escherichia coli*: Nucleotide Sequence of the *supP*(Am) Suppressor Gene," *Journal of Bacteriology* 161(1):219-222. The Examiner alleges that Thorbjarnardóttir *et al.* discloses leucyl-tRNA species comprising the consensus CU(X)nXXXAA, and further, where the leucyl-tRNA species of Thorbjarnardóttir *et al.* have suppression activity, and thus may be presumed to possess at least 25% suppression activity as recited in claims 17 and 26.

Applicants respectfully disagree, and traverse this rejection. Solely for the purpose of advancing the prosecution of the present application, and without acquiescing to the Examiner's

rejection, the Applicants have amended claims 17 and 26. Rebuttal to the Examiner's rejection is made in view of the amended forms of claims 17 and 26. In order for a reference to anticipate a claim, the reference must teach each and every element of the claim (MPEP 2131).

Thorbjarnardóttir *et al.* falls short of anticipating the currently amended form of claims 17 and 26.

The amended forms of claims 17 and 26 no longer define a genus of leucyl-O-tRNA molecules using the CU(X)<sub>n</sub>XXXAA consensus limitation or the at least 25% suppression activity limitation. The amended forms of claims 17 and 26 now define the members of the genus of leucyl-O-tRNA molecules specifically by sequence limitation, *i.e.*, a leucyl-O-tRNA comprising a nucleotide sequence selected from SEQ ID NOS: 1, 2, 4-7 and 12. Each of these members is clearly defined in the specification; see Example 2 starting at paragraph **0218**. Thorbjarnardóttir *et al.* does not teach the nucleotide sequences of SEQ ID NOS: 1, 2, 4-7 and 12.

The Examiner rejected claim 26 under 35 U.S.C. § 102(b) as allegedly anticipated by Thorbjarnardóttir *et al.* in view of the expression "derived from." The Examiner states that although the leucyl O-tRNA is derived from *Halobacterium sp NRC-1* and the leucyl O-RS is derived from *Methanobacterium thermoautotrophicum*, the expression "derived from" is not sufficiently limiting to avoid reading on Thorbjarnardóttir *et al.*

Applicants respectfully disagree, and traverse this rejection. As discussed above, Applicants have amended claim 26. The amended form of claim 26 defines the members of the genus of leucyl-O-tRNA molecules specifically by sequence limitation, *i.e.*, a leucyl-O-tRNA comprising a nucleotide sequence selected from SEQ ID NOS: 1, 2, 4-7 and 12. Thorbjarnardóttir *et al.* does not teach the nucleotide sequences of SEQ ID NOS: 1, 2, 4-7 and 12. Therefore, Thorbjarnardóttir *et al.* falls short of anticipating the currently amended form of claim 26.

Applicants assert that the amended forms of the claims are novel, and it follows that each claim that depends from the novel independent claims 17 and 26 must also be novel. Because Thorbjarnardóttir *et al.* does not teach each element of the claimed invention, Applicants respectfully request that this rejection be withdrawn.

35 U.S.C. § 102(e)

In the Office Action, claims 17-26 were rejected under 35 U.S.C. § 102(e) as allegedly anticipated by WO 2002/085923 to Schultz *et al.*, entitled “IN VIVO INCORPORATION OF UNNATURAL AMINO ACIDS.” The Examiner alleges that WO 2002/085923 discloses an O-tRNA identical in sequence to the O-tRNA of SEQ ID NO: 3 of the present application. The Examiner also alleges that WO 2002/085923 discloses an O-RS identical in sequence to the O-RS of SEQ ID NO: 15 of the present application.

Solely for the purpose of advancing the prosecution of the present application, and without acquiescing to the Examiner’s rejection, the Applicants have amended claims 17 and 26. Rebuttal to the Examiner’s rejection is made in view of the amended forms of claims 17 and 26. In order for a reference to anticipate a claim, the reference must teach each and every element of the claim (MPEP 2131). The rejection does not establish how the amended forms of the claims are taught by the cited art.

The amended forms of independent claims 17 and 26 define the members of the genus of leucyl-O-tRNA molecules specifically by structural limitation, *i.e.*, a leucyl-O-tRNA comprising a nucleotide sequence selected from SEQ ID NOS: 1, 2, 4-7 and 12. Each of these O-tRNA sequences is defined in the present specification. The O-tRNA of SEQ ID NO: 3 has been excluded from the genus of O-tRNA molecules recited in the amended forms of claims 17 and 26.

Applicants assert that the amended forms of claims 17 and 26 are novel, and it follows that each claim that depends from claims 17 and 26 must also be novel. Applicant respectfully requests that this rejection be withdrawn.

In the Office Action, claims 17-19, 21 and 22-26 were rejected under 35 U.S.C. § 102(e) as allegedly anticipated by US Patent No. 7,083,970 to Schultz *et al.*, entitled “Methods and Compositions for the Production of Orthogonal tRNA-Aminoacyl tRNA Synthetase Pairs.” The Examiner alleges that US 7,083,970 discloses an O-tRNA identical in sequence to the O-tRNA of SEQ ID NO: 3 of the present application.

Solely for the purpose of advancing the prosecution of the present application, and without acquiescing to the Examiner’s rejection, the Applicants have amended claims 17 and 26. Rebuttal to the Examiner’s rejection is made in view of the amended forms of claims 17 and 26. US 7,083,970 falls short of anticipating the currently amended claims 17 and 26.

The amended forms of claims 17 and 26 no longer define a genus of leucyl-O-tRNA molecules using the CU(X)<sub>n</sub>XXXAA consensus limitation or the at least 25% suppression activity limitation. The amended forms of independent claims 17 and 26 now define the members of the genus of leucyl-O-tRNA molecules specifically by structural limitation, *i.e.*, a leucyl-O-tRNA comprising a nucleotide sequence selected from SEQ ID NOS: 1, 2, 4-7 and 12. Each of these O-tRNA sequences is defined in the present specification. The O-tRNA of SEQ ID NO: 3 has been excluded from the genus of O-tRNA molecules recited in the amended forms of claims 17 and 26, overcoming the apparent basis of the rejection.

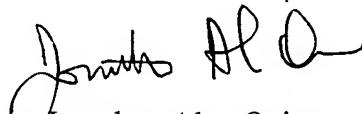
Applicants assert that the amended forms of claims 17 and 26 are novel, and it follows that each claim that depends from claims 17 and 26 must also be novel. Applicant respectfully requests that this rejection be withdrawn.

### CONCLUSION

In view of the foregoing, Applicants believe that all claims now pending in this application are definite, novel and are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

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### Attachments:

- 1) a transmittal sheet; and
- 2) a receipt acknowledgement postcard.